REMARKS

Claims 1 and 3 have been amended to clarify that the cells or tissue are infected with two separate sets of viral particles. Claim 2 has been amended to correct a grammatical error. The amendments are fully supported by the original claims and the specification and do not contain new matter. Support for infection with two independent sets of viral particles can be found in the specification at paragraphs [0021] ("results with two independent virus block stocks are shown . . ."); [0068] (describing set "(a)" and set "(b)" of viral particles); and [0079] (Example 4, showing BHK cells were infected with antisense virus stocks or sense virus stocks). Claims 7-8 have been withdrawn by the Examiner as non-elected. Thus, claims 1-6 are pending.

The Applicants expressly rebut any presumption that the Applicants have surrendered any equivalents under the doctrine of equivalents and expressly state that the claims, as amended, are intended to include and encompass the full scope of any equivalents as if the claims had been originally filed and not amended.

Claim Rejections Under 35 USC § 112, 1st Paragraph: Indefiniteness

Claims 1-6 have been rejected under 35 USC §112, first paragraph for indefiniteness. According to the Examiner, it is unclear if infection occurs with viral particles containing both sense and antisense RNA strands or if infection occurs with a first set of viral particles with the sense RNA strand and a second set of viral particles with the antisense RNA strand. In response, the claims have been amended to clarify that the cells or tissue are infected with two separate sets of viral particles (one sense and the other antisense). Accordingly, this rejection is now moot and the Applicants respectfully request that the rejection be withdrawn.

Claim Rejections Under 35 USC § 102

Claims 1, 2, 4 and 6 are rejected under 35 U.S.C. § 102(b) as being anticipated by Ding. The Examiner asserts that Ding teaches "a process for inhibiting expression of a viral gene in cells or tissues, in vitro, by administration of viral particles comprising a sense ssRNA or antisense ssRNA targeted to viral genes . . ." and that the cells are infected with equal amounts of viral particles and that the RNA sequences are at least 50 bases in length. The Examiner cites pages 3271 and 3272 (second column, first paragraph) of the material and methods section of Ding.

In order for a reference to anticipate a claim under 35 U.S.C. § 102, the reference must disclose every element or step of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently, in a single prior art reference." *See* MPEP § 2131.

Here, Ding fails to disclose all of the claim elements. Ding does not teach the step of administering to cells or tissue both (a) a first set of viral particles consisting essentially of single stranded ribonucleic acid (ss RNA) which expresses a sense RNA strand (not antisense), and (b) a second set of viral particles consisting essentially of ss RNA which expresses an anti-sense RNA strand (not sense).

In contrast, Ding teaches the infection of cells with only a single set of viral particles for each experiment. See page 3274 in Ding under the heading "HIV-1 susceptibility of stable MT4 transductants" which indicates that one group of cells was infected with viral particles containing MoTiN (control); a separate group of cells was infected with viral particles containing MoTiN-TRΨ^{e+}; a separate group of cells was infected with viral particles containing MoTN; and another separate group of cells was infected with viral particles containing MoTN-TR$\Psi^{e+/-}$. Similarly, on page 3275 under the heading "HIV-1 susceptibility of human PBL transductants," Ding indicates that separate groups of human PBLs were transduced with a single set of viral particles (each set

separately containing either MoTN, MoTN-TR$\Psi^{e+/-}$, or MoTN-Ψ^{-}. No more than one set of viral particles was administered to any one group of cells.

In no instance does Ding teach infecting the same group of cells with two sets of viral particles: a first set of viral particles with RNA expressing the sense RNA strand (not anti-sense), and a second set of viral particles with RNA expressing the anti-sense RNA strand (not sense).

Accordingly, because Ding fails to disclose the all the elements or steps of the claimed invention, the rejection under 35 U.S.C. § 102 should be withdrawn.

Claim Rejections Under 35 USC § 103

Claims 1-4 and 6 are rejected under 35 U.S.C. § 103 as being unpatentable over Ding in view of Lundstrom. The Examiner asserts that although Ding does not teach the use of an alphavirus, it would have been obvious to one of ordinary skill in the art to substitute the virus in Ding with the alphavirus as taught by Lundstrom.

Claims 1-2 and 4-6 are also rejected under 35 U.S.C. § 103 as being unpatentable over Ding in view of Fire. The Examiner asserts that, although Ding does not disclose targeting a developmental gene, oncogene, a tumor suppressor gene or an enzyme, it would have been obvious to one of ordinary skill in the art to target such developmental gene, oncogene, tumor suppressor gene, or enzyme as taught by Fire.

A. No Prima Facie Case of Obviousness Has Been Established

A *prima facie* case of obviousness has not been established because Ding (taken alone or in combination with Lundstrom and/or Fire) does not teach or suggest all the claim limitations. Under MPEP § 2143.03 in order to establish a *prima facie* case of obviousness of a claimed invention, all the claim limitations must be taught or

suggested by the prior art. If the prior art references do not disclose or suggest all of the claim limitations either by themselves or in combination with each other, there can be no *prima facie* case of obviousness.

Here, the deficiencies in Ding are not cured by the addition of either Lundstrom or Fire. Neither Ding, nor Lundstrom nor Fire teach or suggest the step of administering to cells or tissue both (a) a first set of viral particles consisting essentially of single stranded ribonucleic acid (ss RNA) which expresses a sense RNA strand (not antisense), and (b) a second set of viral particles consisting essentially of ss RNA which expresses an anti-sense RNA strand (not sense).

As stated above, Ding teaches the infection of cells with only a single set of viral particles for each experiment. See page 3274 in Ding under the heading "HIV-1 susceptibility of stable MT4 transductants" which indicates that one group of cells was infected with viral particles containing MoTiN (control); a separate group of cells was infected with viral particles containing MoTiN-TRΨ^{e+} (sense); a separate group of cells was infected with viral particles containing MoTN (control); and another separate group of cells was infected with viral particles containing MoTN-TR$\Psi^{e+/-}$ (sense and antisense copackaged within the same vector). Similarly, on page 3275 under the heading "HIV-1 susceptibility of human PBL transductants," Ding indicates that separate groups of human PBLs were transduced with a single set of viral particles [each set separately containing either MoTN (control); MoTN-TR$\Psi^{e+/-}$ (sense and antisense copackaged within the same vector); or MoTN-Ψ^{-} (antisense). No more than one set of viral particles was administered to any one group of cells.

In no instance does Ding, Lundstrom, or Fire teach infecting the same group of cells with two sets of viral particles: a first set of viral particles with RNA expressing the sense RNA strand (not anti-sense), and a second set of viral particles with RNA expressing the anti-sense RNA strand (not sense). Accordingly, there is no teaching in Fire or Johanning that discloses the use of two separate viral particle populations

(wherein one population provides the sense strand instead of the anti-sense strand and the other provides the anti-sense strand instead of the sense strand).

Thus, Ding (taken alone or in combination with Lundstrom or Fire) does not teach or suggest all the claim limitations for each claim of the present invention. Accordingly, a *prima facie* case of obviousness has not been established for this reason alone.

B. There Are Surprising And Unexpected Results

The Examples of the present application surprisingly demonstrate that when the sense and anti-sense fragments are provided by different vectors there is an inhibition of the expression of chromosomal cyclin genes. In contrast, when both sense and anti-sense fragments are provided in the same construct in the same vector inhibition of the expression of chromosomal cyclin genes does not occur (*see* Examples 6 & 7 on page 15 of the specification). Under MPEP § 2144-45, evidence of such surprising and unexpected results rebuts a *prima facie* case of obviousness.

All of the claims of the present invention require that cells or tissue be infected by two different sets of viral particles: one set providing the sense RNA and the other providing the anti-sense RNA. As shown in Example 7 (page 15 of the specification), when both sense and anti-sense sequences are cloned into the same construct in the same vector, there was no inhibition of the target gene(s) after infection. In contrast, as shown in Example 6, when the sense and anti-sense sequences are cloned separately into separate vector populations, there was inhibition of the target gene(s) after infection (which was even more potent than inhibition of cell growth by antibiotics [neomycin and zeocin], *see* page 15 of the specification). This represents surprising and unexpected results. Accordingly, these surprising and unexpected results rebut any assertion that the claimed invention is obvious.

For all of the above reasons, the Applicants respectfully request that the rejection under 35 U.S.C. § 103 be withdrawn.

Conclusion

Entry of the foregoing remarks and amendments is respectfully requested. A Petition for Extension of Time is submitted herewith (in duplicate) accompanied by the appropriate provision authorizing payment of the required fee. No other fee is believed to be due in connection with the filing of this Amendment. However, if any other fee is deemed necessary, authorization is given to charge the amount of any such fee to Deposit Account No. 08-2525.

Respectfully submitted,

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